Mediterranean Journal of Medicine & Medical Sciences
ISSN: 3107-2720
Mediterr J Med Med Sci
doi: 10.5281/zenodo.22177206
https://mmj.org.ly

ORIGINAL RESEARCH article

In vitro evaluation of the inhibitory effect of phenolic acids on protein glycation: A potential strategy for reducing diabetic complications

Asma O. Jebril [*], **Hamza Atiya**, and **Esraa A. Eskander**

Department of Biochemistry and Clinical Biochemistry, Faculty of Pharmacy, University of Tripoli, Tripoli, Libya
[*] Author to whom correspondence should be addressed

Received: 18-05-2026, **Accepted:** 28-08-2026, **Published online:** 31-08-2026

Copyright© 2026. This open-access article is distributed under the *Creative Commons Attribution License*, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

HOW TO CITE THIS

Jebril AO, et al. *In vitro* evaluation of the inhibitory effect of phenolic acids on protein glycation: A potential strategy for reducing diabetic complications. Mediterr J Med Med Sci. 2026; 2(3): 115-125. [Article number: 53]. https://doi.org/10.5281/zenodo.22177206

Keywords: Bovine serum albumin, gallic acid, ferulic acid, protein carbonyl content, glycated serum albumin

Abstract: Advanced glycation end-products are harmful compounds formed through non-enzymatic reactions between sugars and proteins. Their accumulation, particularly under hyperglycemic conditions, contributes significantly to oxidative stress and chronic complications in diabetes mellitus. Natural compounds with antioxidant and antiglycation properties, such as phenolic acids, are increasingly being investigated as preventive agents. This study aimed to evaluate and compare the inhibitory effects of ferulic acid and gallic acid on AGE formation and oxidative protein damage in an *in vitro* bovine serum albumin (BSA) glucose model as a potential strategy to mitigate diabetes-related complications. BSA was incubated with 1.10 M glucose at 37 °C for 2, 4, and 6 weeks, with or without phenolic acids (gallic acid or ferulic acid) at various concentrations (1-10 µM). The formation of fluorescent Advanced glycation end-products was assessed using Spectrofluorometry (Ex/Em: 360/460 nm), while protein carbonyl content-an indicator of oxidative damage-was measured via the DNPH assay (absorbance at 375 nm). Gallic acid and ferulic acid significantly reduced AGE fluorescence and protein carbonylation compared to the glycated control. Gallic acid showed more consistent inhibition across most time points and concentrations. Ferulic acid was less effective at earlier stages but exhibited delayed protective effects at week six. The difference in inhibitory activity may be attributed to structural variations, particularly the number and position of hydroxyl groups influencing BSA binding affinity. Gallic acid demonstrated superior antiglycation and antioxidant effects compared to ferulic acid under identical experimental conditions. These findings support the potential application of phenolic acids as natural inhibitors of glycation-related protein damage.

Introduction

Advanced glycation end-products (AGEs) are formed through a non-enzymatic reaction known as the Maillard reaction, the primary pathway leading to the formation of AGEs between reducing sugars (such as glucose) and free amino groups on proteins, lipids, or nucleic acids. This process begins with the formation of reversible Schiff bases and Amadori products, which over time undergo oxidation and rearrangement to form irreversible AGEs [1-4]. Unlike enzymatic glycosylation, glycation is unregulated and enhanced under hyperglycemic conditions. The accumulation of AGEs in tissues promotes oxidative stress, inflammation, and structural damage, playing a major role in the development of diabetic complications such as retinopathy, nephropathy, neuropathy, and cardiovascular disease [5]. AGE formation is particularly problematic because it induces structural and functional

alterations in proteins. Glycated proteins often lose their native conformation, become resistant to proteolytic degradation, and may acquire pro-inflammatory properties. In structural proteins such as collagen, AGEs contribute to tissue stiffness and reduced elasticity, while in enzymes and transport proteins, glycation may directly impair biological activity and disrupt metabolic regulation [6]. The formation (**Figures 1** and **2**) and accumulation of AGEs in the human body are influenced by endogenous (internal metabolic) and exogenous (external/environmental) factors. These factors accelerate non-enzymatic glycation reactions and impair AGE clearance, ultimately contributing to tissue damage and chronic disease.

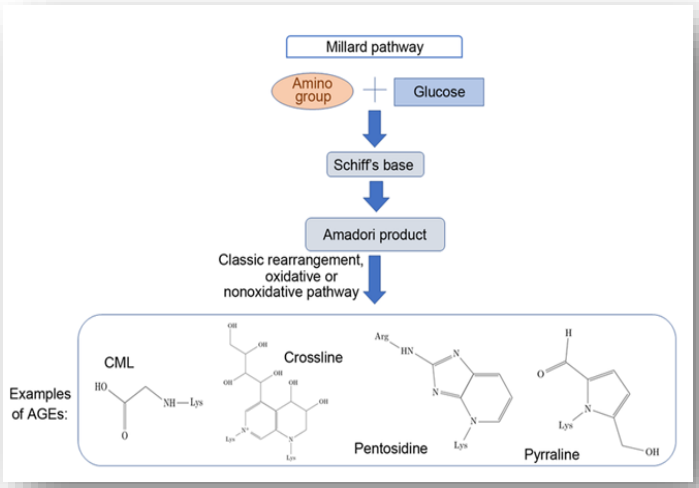

Figure 1: Formation of advanced glycation endproducts

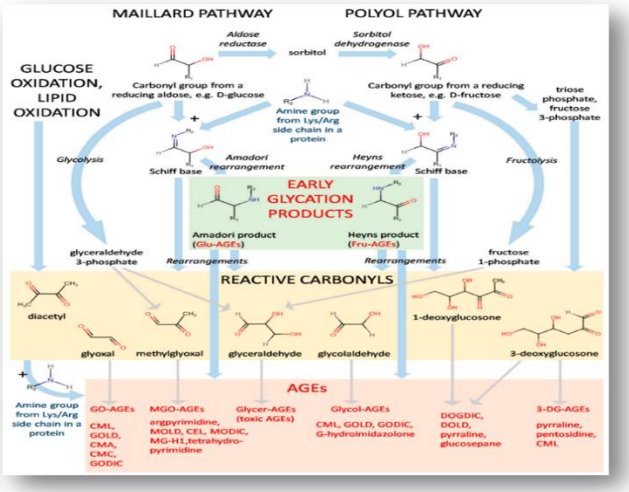

Figure 2: Glycation *p*athway

Type 1 diabetes mellitus (T1DM) or Insulin-dependent diabetes mellitus is characterized by autoimmune-mediated destruction of pancreatic β-cells, leading to absolute or near-absolute insulin deficiency. This results in a persistent post-absorptive metabolic state, characterized by elevated blood glucose levels and increased ketogenesis. In contrast, type 2 diabetes mellitus (T2DM) or non-insulin-dependent diabetes mellitus is primarily defined by peripheral insulin resistance. Although insulin is often present in normal or even elevated levels, the cellular response is impaired, disrupting the normal transition between post-absorptive and post-prandial states. Over time, β-cell dysfunction may also develop, further exacerbating hyperglycemia [7]. Sustained chronic hyperglycemia in both types of diabetes alters normal metabolic processes including glycolysis, glycogenesis, and lipogenesis, and activates pathological pathways. One major consequence is the non-enzymatic glycation of biomolecules, leading to the formation of AGEs [8, 9]. Despite the inherent chemical stability of AGEs, the human body possesses multiple sophisticated detoxification mechanisms to minimize their accumulation and mitigate their toxicity. However, the efficacy of these crucial clearance systems can become compromised with age or in pathological states such as diabetes mellitus and chronic kidney disease.

In recent years, there has been growing interest in polyphenols, a large group of naturally occurring plant metabolites characterized by multiple phenol units. These compounds are widely distributed in fruits, vegetables, tea, coffee, and whole grains and are well known for their potent antioxidant properties, which allow them to neutralize free radicals and reduce oxidative stress, a key contributor to chronic diseases such as diabetes and its complications [10]. Polyphenols are classified into four main groups: Flavonoids, phenolic acids, lignans, and stilbenes (**Figure 3**). Among these, phenolic acids, notably ferulic acid (FA) and gallic acid (GA) (**Figure 4**), are abundant in grains and fruits and have attracted attention for their anti-inflammatory, antioxidant, and anti-glycation properties [11]. Due to these bioactive properties, phenolic acids such as FA and GA have been studied

for their potential to inhibit the formation of AGEs, which are known to play a critical role in the pathogenesis of diabetic complications. Their ability to interfere with glycation pathways is believed to be mediated through their modulation of oxidative stress and inflammatory signaling [8].

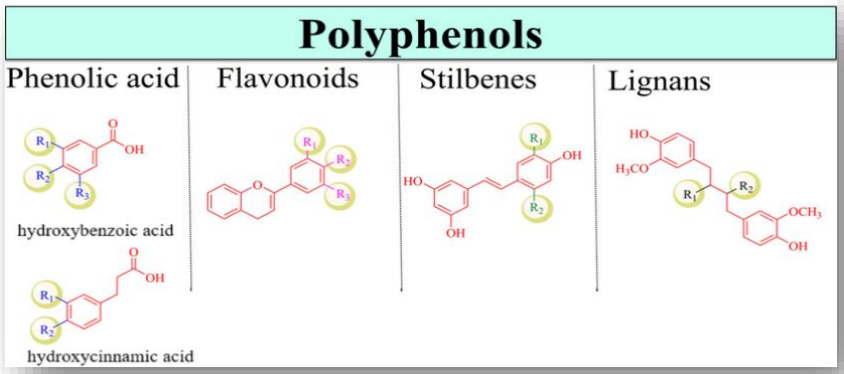

Figure 3: Polyphenolic compounds

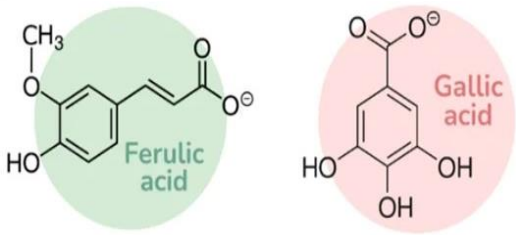

Figure 4: Gallic acid and ferulic acid

Materials and methods

Bovine serum albumin (BSA) glycation: The glycation assay was conducted following a modified protocol as previously described [12]. All samples were prepared using fresh phosphate-buffered saline (PBS) (20.0 mM, pH 7.4) supplemented with 0.2% sodium azide (NaN_3) to prevent microbial growth. BSA (50.0 mg/mL) was dissolved in PBS (20.0 mM, pH 7.4) and incubated with glucose (1.1 M) in phosphate buffer and sodium azide (0.2%). The phenolic acids (10.0 mM), GA, and FA (the stock solution of Fer was prepared and dissolved in the least amount of DMSO, then completed with PBS). Different concentrations of phenolic acids were added to the BSA mixture with final concentrations of 1, 2, 3, 4, 5, and 10 µM and were incubated at 37 °C for 2, 4, and 6 weeks. A control reaction was without phenolic acid and represented 100% glycation. The final concentration effect of DMSO as a solvent for phenolic acids was evaluated. Light protection was ensured by wrapping tubes in aluminum foil and storing them in closed incubators. Post-incubation, samples were frozen at – 20.0 °C until further analysis.

Determination of protein carbonyl content: Protein carbonyl content, as an indicator of protein oxidation, was quantified using the 2,4-dinitrophenylhydrazine (DNPH) assay [10] of each sample; 0.5 mL was mixed with an equal volume of 10.0 mM DNPH solution and incubated in the dark at room temperature for one hour to allow hydrazone formation.

$$\mathbf{R–C=O\ (carbonyl\ group) + H_2NNH–C_6H_3(NO_2)_2 \rightarrow R–C=N–NH–C_6H_3(NO_2)_2 + H_2O}$$

This reaction forms a stable hydrazone product, which absorbs at 375 nm and is measured spectrophotometrically. After incubation, protein was precipitated by adding 0.5 mL of cold 20.0% trichloroacetic acid (TCA) to the tubes and kept on ice for five minutes for proteins to precipitate out. The mixture was centrifuged at 6000 × g for 10 min at 4.0 °C, and the supernatant was discarded. The resulting pellet was washed three times with a 1: 1 (v/v) mixture of ethanol and ethyl acetate to remove unreacted DNPH, lipids, and excess glucose. Each wash was followed by centrifugation at 6000 × g for 15 min at 4.0 °C [11]. The final pellet was dissolved in 1.0 mL of 8.0 M urea and incubated for 15 - 30 min at room temperature with intermittent mixing to ensure complete solubilization. The absorbance of the resulting solution was measured at 375 nm using a UV-Vis

Spectrophotometer (JENWAY 6505 UV/Vis, UK). The carbonyl content was calculated using the molar extinction coefficient of 22,000 $M^{-1} \cdot cm^{-1}$ for DNPH and expressed as nmole of carbonyl/mg of protein by using the following equation:

$$\textbf{Carbonyl content (nmol/mg)} = (A_{375} \times \times 10^9) / (\varepsilon \times \textbf{protein concentration})$$

A_{375}: Absorbance at 375 nm, ε: molar extinction coefficient of DNPH (usually 22,000 M^{-1} cm^{-1}), and protein concentration: in mg/mL

Measurement of Fluorescent AGEs: The glycation process leads to the formation of fluorescent AGEs. So, these products were measured at an excitation wavelength of 360 nm and an emission maximum of 460 nm. A 2.0 mL aliquot of each sample was taken directly (without dilution) and transferred to Eppendorf test tubes (2.0 mL) [11]. The results were expressed as the fluorescent intensity.

Statistical analysis: All statistical analyses were performed using GraphPad Prism version 8. For each time point, the mean values and corresponding *p*-values were calculated. Comparisons between two groups, namely week 2 vs. week 4, week 2 vs. week 6, and week 4 vs. week 6, were conducted using the unpaired *t*-test. This statistical method was selected because it is appropriate for evaluating differences between two independent groups. Most *p*-values were less than 0.05 and were therefore considered statistically significant, although a few comparisons did not reach statistical significance.

Results

Effect of phenolic acids on protein carbonyl contents: The effect of phenolic acids (GA and FA) on protein carbonyl contents is presented in **Figures 5, 6,** and **7**. The levels of protein carbonyl in glycated BSA significantly increased after two weeks of incubation. In contrast, protein carbonyl in glycated BSA started to decline after four weeks.

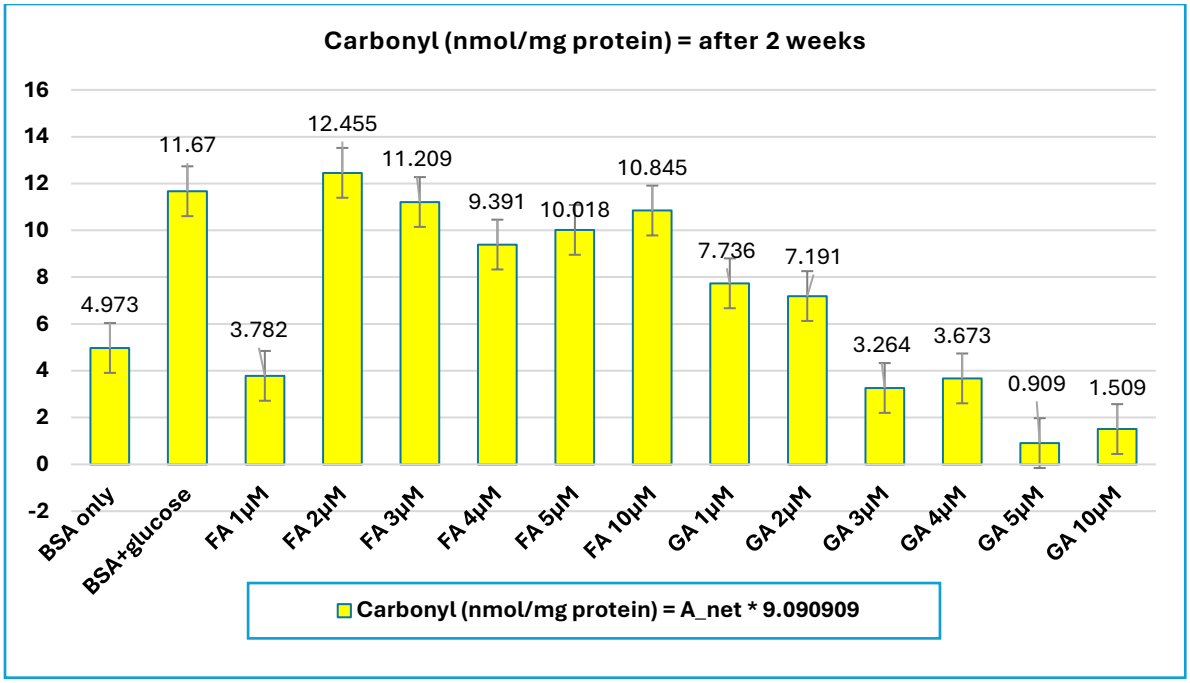

Figure 5: Effect of gallic acid and ferulic acid on protein carbonyl contents after two weeks

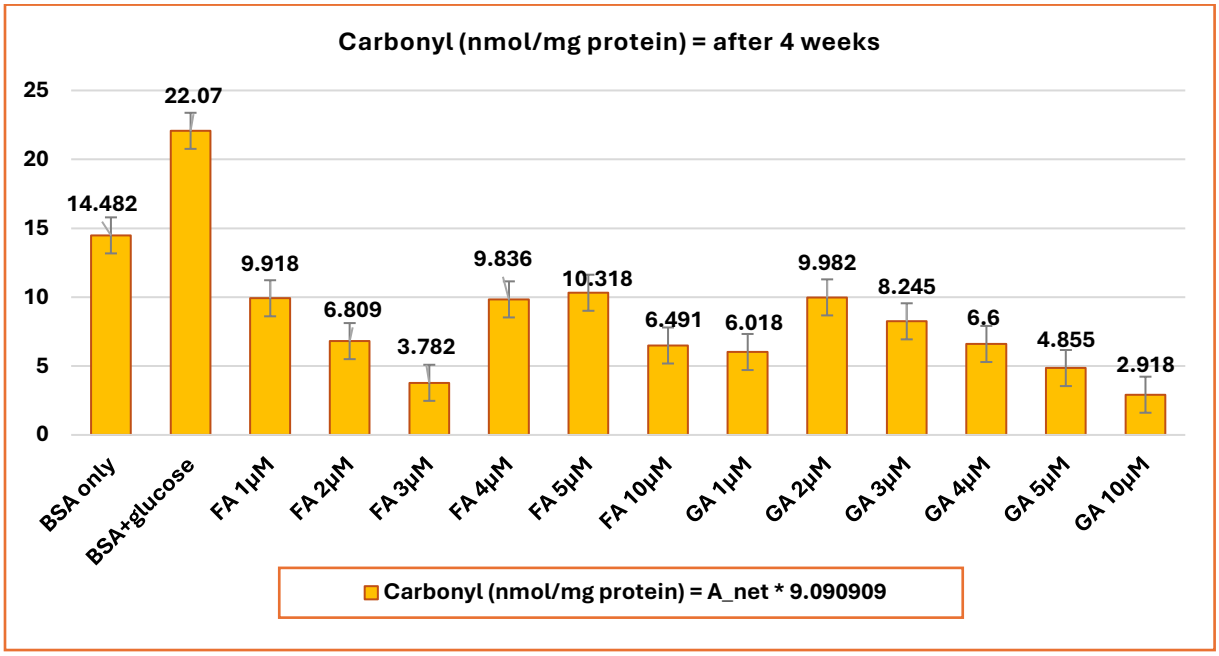

Figure 6: Effect of gallic acid and ferulic acid on protein carbonyl contents after four weeks

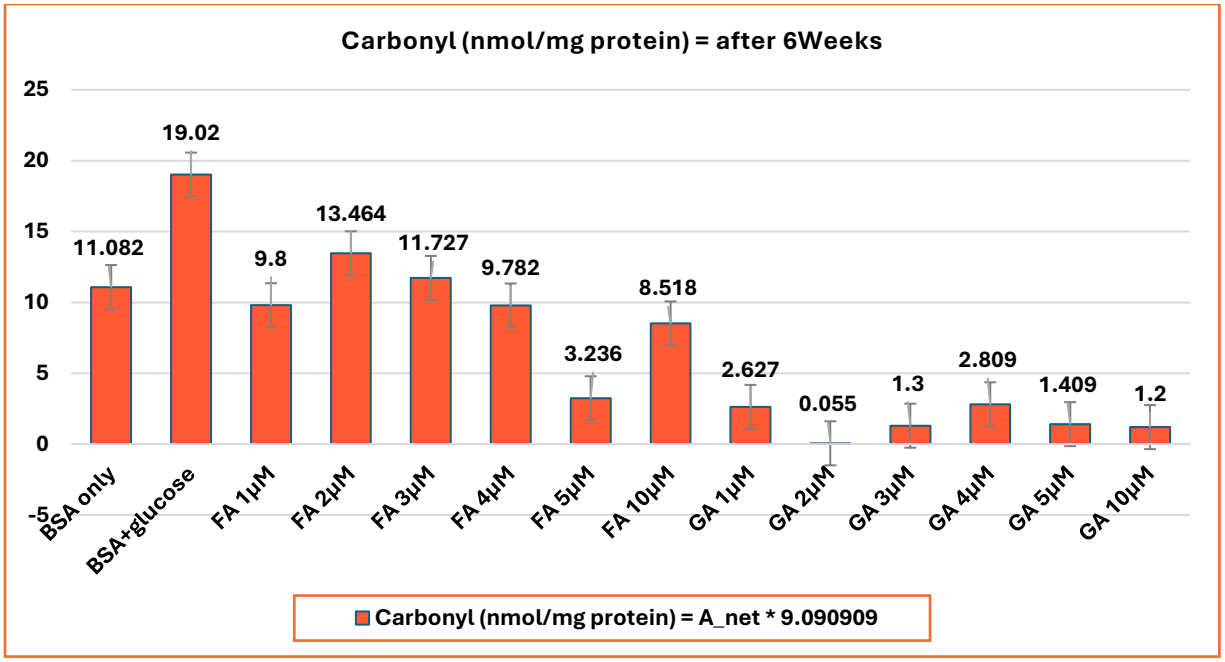

Figure 7: Effect of gallic acid and ferulic acid on protein carbonyl contents after six weeks

The addition of GA and FA with different concentrations (1, 2, 3, 4, 5, and 10 µM) decreased protein carbonyl content levels of BSA significantly ($p < 0.05$) after 2, 4, and 6 weeks of incubation by GA for all concentrations, while FA blocked protein carbonyl content levels of BSA significantly ($p < 0.05$) after 4 and 6 weeks of incubation but was unable to inhibit protein carboxylation after four weeks of incubation. However, concentrations of 2, 3, and 10 μM of GA blocked protein carbonylation in glycated BSA significantly after six weeks of incubation (**Figure 8**). These findings are consistent with our data, demonstrating that GA was more effective in inhibiting protein carbonylation and AGE formation compared to FA. The enhanced activity of GA may be attributed to the presence of three hydroxyl groups in its structure, which confer strong free radical scavenging properties.

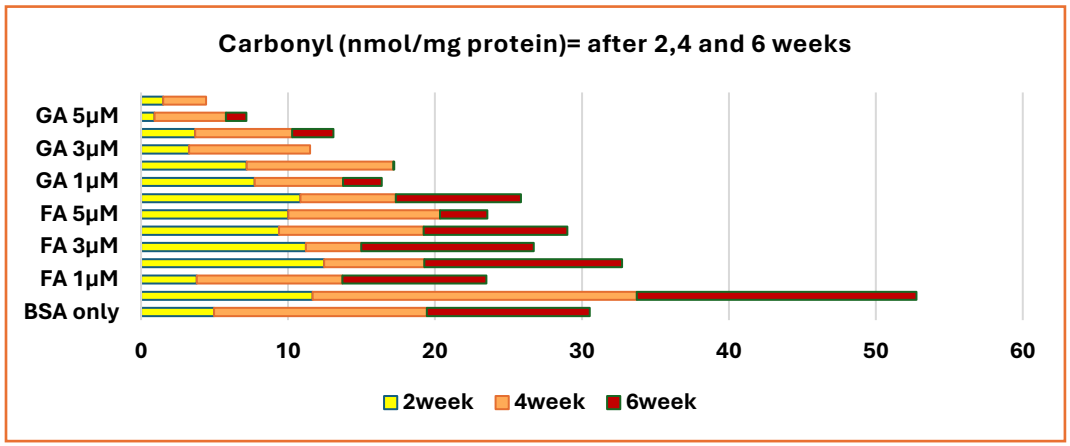

Figure 8: Effect of gallic acid and ferulic acid on protein carbonyl contents after 2, 4 and 6 weeks

However, while the number of hydroxyl groups plays a significant role, their position on the benzene ring is also critical. For example, hydroxyl groups at the 2-position and 4-position of the aromatic ring have been reported to exert positive and negative effects, respectively, on binding affinity to serum albumin. Statistically, the difference in glycation formation content (nmol/mg protein) between two and four weeks resulted in a significant difference for GA (3 and 5.0 µM) and FA (1, 2, 3, and 10 µM) ($p < 0.05$), which means the effect of the phenolic acids in these concentrations declines over time from two to four weeks (**Figure 9**). After six weeks of incubation, the results showed a significant difference ($p < 0.05$) between four and six weeks for GA (2.0 and 3.0 µM) and for FA (2, 3, and 5 µM), which means there is a rise in carbonyl content once again after four weeks.

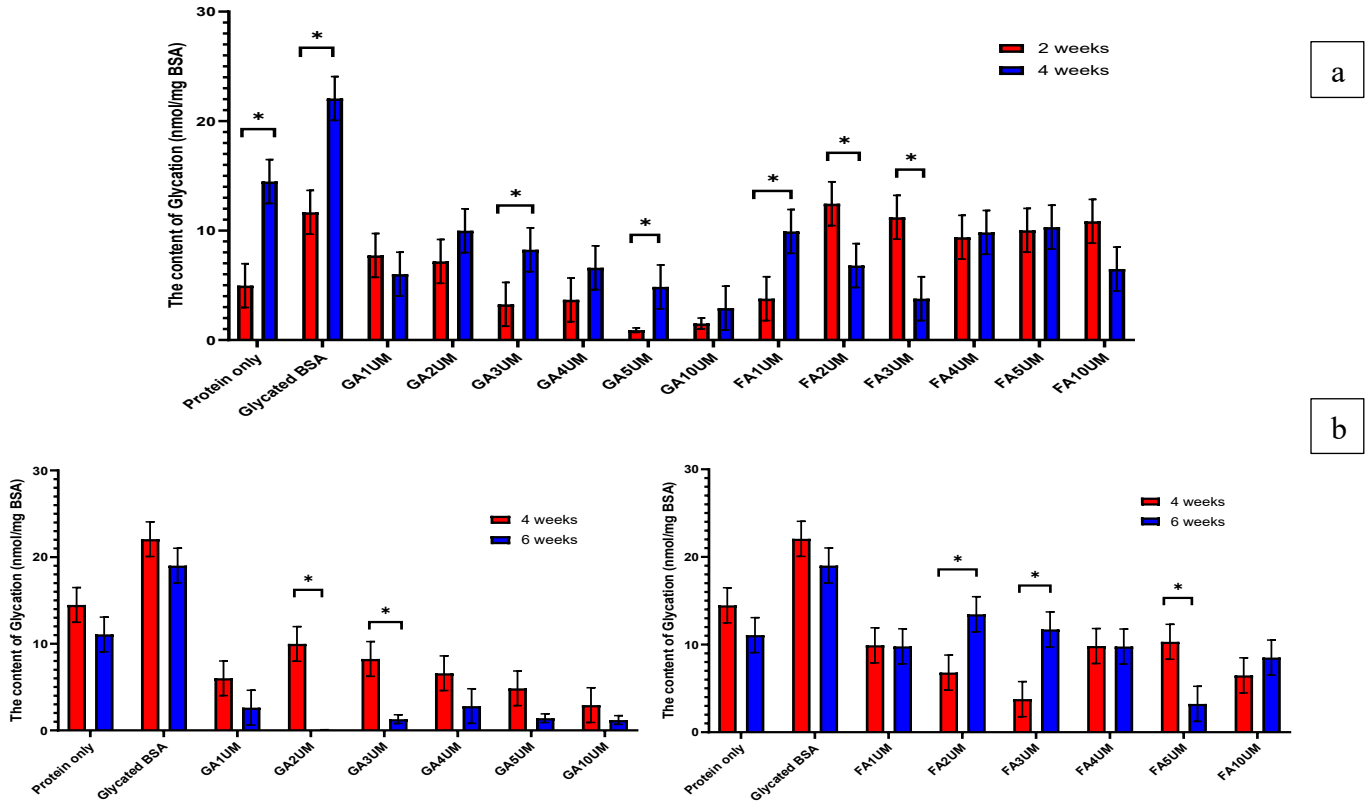

Figure 9: The statistical analysis of glycation formation content (a) between 2- and 4-week compression (b). The statistical analysis of glycation formation content between 4 and 6 weeks of compression for FA and GA (BSA: bovine serum albumin, Gal: gallic acid, Fer: ferulic acid)

The effect of phenolic acids on BSA-derived fluorescence: AGEs have fluorescent properties; the fluorescence spectroscopy method was used to evaluate the extent of AGEs formation fluorescence intensity of BSA and glucose in the presence or absence of phenolic acids. At three incubation times, the fluorescence intensity of the mixture of glucose and BSA increased significantly. In this study, the reaction of glucose with BSA was used as a model for investigating the protective effects of phenolic acids on protein glycation. Treatment with GA and FA decreased the fluorescence intensity, which showed the ability of those phenolic acids to inhibit AGEs formation. After two weeks of incubation, the fluorescence intensity of the mixture of glucose and BSA increased significantly compared with BSA (**Table 1**). Whereas the addition of GA and FA (1, 2, 3, 4, 5, and 10 µM) decreased the fluorescence intensity in comparison with glycated BSA. During the first two weeks, a marked decrease in fluorescent AGE levels was observed across all concentrations of GA and FA, as illustrated in **Figure 10**. After four weeks, the graph in **Figure 10** showed that GA (2, 3, 4, 5 and 10 μM) continued to decrease the fluorescence intensity in comparison with two weeks. In GA, at the fourth week, a continued reduction in fluorescent AGE levels was evident at all GA concentrations, with the exception of the 1.0 µM GA group, which did not show a significant decrease.

Table 1: Percentage of glycation after 2, 4, and 6 weeks

	Percent of glycated BSA (%)			Raw Fluorescence		
Sample	2W.	4W.	6W.	2W.	4W.	6W.
Protein only	55.0±0.39	68.0±0.09	65.0±0.16	117.0±1.18	145.2±0.065	117.9±0.057
Glycated BSA	99.5±0.50	94.0±0.6	99.0±1.0	213.3±0.052	213.35±0.002	181.0±0.024
GA1UM	64.0±0.80	102.0±0.94	88.0±0.71	138.0±0.254	219.62±0.002	160.0±0.585
GA2UM	55.0±0.89	92.0±1.0	94.0±0.23	119.2±0.053	198.0±0.409	170.57±0.002
GA3UM	54.0±0.28	96.0±0.3	93.0±0.55	115.8±0.001	205.4±0.065	169.3±0.041
GA4UM	53.0±0.33	99.0±0.17	78.0±1.09	113.7±0.085	211.0±0.577	143.1±0.66
GA5UM	57.0±0.48	99.0±0.64	87.0±0.91	122.6±0.042	212.5±0.076	159.0±0.134
GA10UM	57.0±0.58	96.0±0.12	106.0±1.88	122.8±0.052	205.0±0.079	195.2±0.089
FA1UM	67.0±0.86	105.0±0.45	108.1±0.06	144.0±0.778	224.9±0.074	194.0±1.796
FA2UM	60.0±0.06	98.0±0.67	92.0±0.07	128.0±0.144	210.0±0.510	166.0±0.673
FA3UM	57.0±0.50	97.50±1.17	92.0±0.61	122.0±0.678	210.5±0.010	166.0±1.643
FA4UM	-	90.0±0.67	88.0±1.36	-	193.0±0.450	161.0±0.764
FA5UM	64.0±0.88	99.0±0.53	101.0±0.62	138.4±0.022	212.34±0.002	183.5±0.458
FA10UM	63.0±0.67	84.0±0.10	69.0±0.53	135.85±0.001	179.4±0.033	125.8±0.073

For FA-treated samples, a decrease in fluorescent AGE levels was also noted at week four. However, the reduction was relatively modest at concentrations of 1.0 µM and 3.0 µM FA. GA continued to exhibit a notable inhibitory effect on fluorescent AGE formation at all concentrations, except at 4.0 µM, where the decrease was not apparent. In contrast, FA-treated samples did not demonstrate a clear or consistent reduction in fluorescent AGE levels during the sixth week.

The fluorescence (% of glycated BSA): To evaluate the extent of protein glycation, the formation of fluorescent AGEs was quantified. Samples were excited at 360 nm, and the emitted fluorescence was measured at 460 nm using an FP-6200 (JASCO, Japan). The fluorescence intensity directly reflects the accumulation of fluorescent AGEs, particularly those resembling pentosidine and crossline structures. The results were expressed as a percentage relative to the glycated BSA group, which was considered 100%. This normalization allows comparison between treated and untreated samples. A decrease in fluorescence percentage indicates an inhibitory effect of the phenolic compounds on AGE formation. The following formula was used to calculate the percentage of fluorescent AGEs:

$$\text{Fluorescent AGEs (\% of Glycated BSA)} = \frac{\text{Fluorescence in treated sample}}{\text{Fluorescence in glycated BSA control}} X100$$

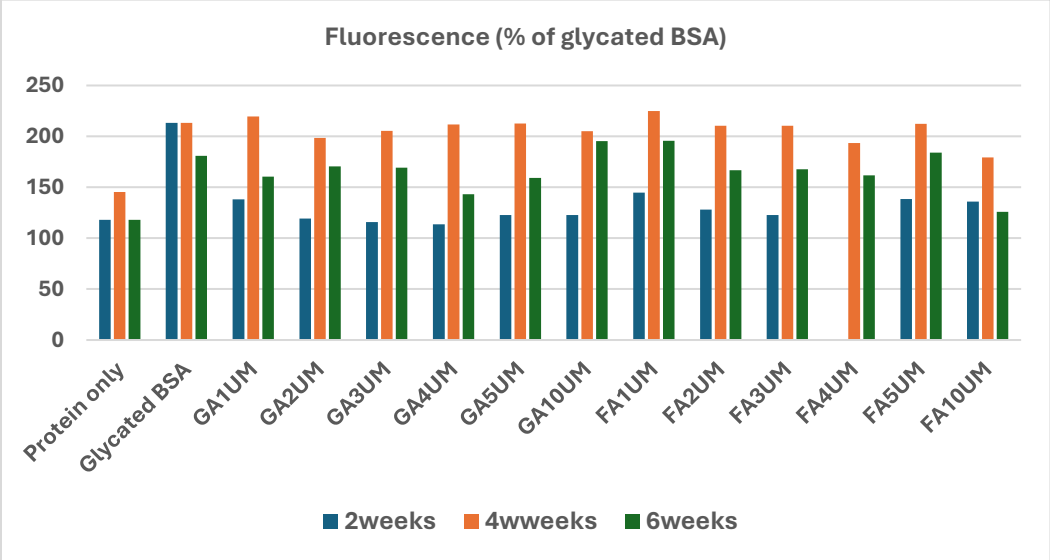

Figure 10: Effect of phenolic acids on inhibition of fluorescence AGEs.
The fluorescent intensity was monitored at excitation and emission wavelengths of 360 and 460 nm.
(*BSA: bovine serum albumin, Gal: gallic acid, Fer: ferulic acid)*

Discussion

Effect of phenolic acids on protein carbonyl contents: The current study demonstrated that GA and FA effectively reduced protein carbonyl content in glycated BSA across all incubation periods (2, 4, and 6 weeks). However, GA exhibited superior inhibitory activity compared to FA, consistent with previous findings demonstrating the potent antiglycation properties of polyphenols [7, 8]. The enhanced efficacy of GA can be attributed to its chemical structure, particularly the presence of three hydroxyl groups on the benzene ring, which confer strong free radical scavenging properties [11, 14]. This structural advantage enables GA to more effectively neutralize reactive oxygen species and prevent oxidative damage to proteins, a key mechanism in inhibiting protein carbonylation [15, 16]. The hydroxyl groups facilitate hydrogen atom donation, terminating free radical chain reactions that would otherwise lead to protein oxidation and carbonyl formation [17]. Notably, whereas FA exhibited considerable inhibition at four and six weeks, it failed to impede protein carboxylation at two weeks at specific doses. This delayed effect may be attributed to the structural differences between the two compounds, with GA possessing three hydroxyl groups compared to FA's single hydroxyl and methoxy substitution pattern [18, 19]. As noted by Rashedinia and others [14], the position of hydroxyl groups on the aromatic ring is critical, with hydroxyl groups at the 2-position and 4-position exerting positive and negative effects, respectively, on binding affinity to serum albumin. The observed biphasic trend in protein carbonyl concentrations, with an initial rise followed by a decrease after four weeks, corresponds with the intricate dynamics of protein glycation and oxidation mechanisms. AGEs formation involves multiple stages, including early glycation, intermediate Amadori product formation, and late-stage AGE accumulation [1, 20]. The subsequent rise in carbonyl content at six weeks suggests that prolonged incubation may lead to secondary oxidative events, consistent with the concept of glycoxidation [21].

Effect of phenolic acids on BSA-derived fluorescence: The fluorescence spectroscopy results confirmed that GA and FA effectively inhibited AGEs formation, as evidenced by decreased fluorescence intensity compared to glycated BSA. This reduction in fluorescence is indicative of decreased accumulation of fluorescent AGEs,

particularly pentosidine- and crossline-like structures [22, 23]. GA demonstrated more consistent inhibitory effects on fluorescence intensity across all concentrations and time points, with the notable exception of the 1 µM concentration at four weeks. This concentration-dependent efficacy suggests that GA's antiglycation activity is dose-dependent, consistent with previous reports [24, 25]. The sustained inhibition by GA may be attributed to its ability to chelate metal ions, scavenge free radicals, and trap reactive carbonyl species, thereby preventing the progression of glycation reactions [16, 19]. In contrast, FA showed more variable results, with modest effects at lower concentrations (1.0 µM and 3.0 µM) during the fourth week and an inconsistent reduction pattern during the sixth week. This variability may reflect differences in the mechanisms of action between the two phenolic acids. While FA has been shown to effectively inhibit glycation through trapping of reactive carbonyl species and metal chelation [16, 23], its efficacy appears to be more dependent on concentration and incubation time.

The statistical analysis in **Figure 9** revealed significant differences between four and six weeks for GA (2.0 and 3.0 µM) and FA (2, 3, and 5 µM), indicating a rise in carbonyl content after the fourth week. This suggests that while phenolic acids provide initial protection against protein glycation, prolonged exposure may overwhelm their inhibitory capacity or, alternatively, that AGEs may undergo further modifications over extended incubation periods. The fluorescence percentage normalization relative to glycated BSA (100%) provided a clear measure of the inhibitory potential of these compounds. The observed decrease in fluorescence percentage in treated samples compared to glycated controls confirms the antiglycation activity of both phenolic acids, consistent with the findings of Sompong et al. [18] and Liu et al. [19]. The findings of the current study have significant implications for understanding the potential protective roles of dietary polyphenols in preventing AGE-related complications in diabetes. Hyperglycemia-induced protein glycation is a major contributor to the pathogenesis of diabetic complications, including nephropathy, retinopathy, neuropathy, and cardiovascular disease [1, 6]. The accumulation of AGEs has been implicated in the development of these complications through activation of the receptor for AGEs, leading to pro-inflammatory and pro-fibrotic signaling cascades [27, 28]. The enhanced activity of GA compared to FA in inhibiting protein carbonylation and AGEs formation suggests that polyphenols with multiple hydroxyl groups may be particularly effective as therapeutic agents or dietary supplements for preventing diabetic complications. GA, abundant in fruits, vegetables, and tea, may be a promising candidate for further investigation as an antiglycation agent [8, 11]. Furthermore, the structure-activity relationship observed in this study provides insights for the development of more effective antiglycation compounds.

Conclusion: This study reveals that gallic acid and ferulic acid effectively inhibit protein carbonylation and AGEs formation in a BSA-glucose glycation model. Gallic acid exhibited superior inhibitory activity, likely attributable to its structural advantages, including three hydroxyl groups that confer potent antioxidant and carbonyl-trapping properties. The findings support the potential therapeutic use of phenolic acids, particularly gallic acid, to prevent AGE-related complications in diabetes and other conditions associated with accelerated protein glycation.

References

1. Singh R, Barden A, Mori T, Beilin L. Advanced glycation end-products: A review. Diabetologia. 2001; 44(2): 129-146. doi: 10.1007/s001250051591
2. Rajab BM, Abodhier AA, Zreiba EN, Abosbea SY. Evaluation of diabetes mellitus type 2 effects on kidney function in Libya. Mediterranean Journal of Pharmacy and Pharmaceutical Sciences. 2023; 3(4): 90-96. doi: 10.5281/zenodo.10396239
3. Nahar N, Chowdhury H, Madzuki IN, Das P, Jamaludin MI, Sharma K, et al. Bibliometric analysis of diabetic retinopathy research using optical coherence tomography (2020-2025): A VOSviewer study. Mediterranean Journal of Medical Research. 2025; 2(4): 239-258. doi: 10.5281/zenodo.17682969

4. Nkollo MI, Onwukwe NA, Emurotu EO, Lucky-Udi H, Ige AE, Ebuehi BI, et al. From pathophysiology to rehabilitation: Addressing low vision in diabetic retinopathy. Mediterranean Journal of Medicine and Medical Sciences. 2026; 2(2): 89-95. doi: 10.5281/zenodo.20685922
5. Departments of Medicine and Pathology and DR and TCAEC of MB. Brownlee Insight Review Articles. 2001. www.nature.com
6. Goldin A, Beckman JA, Schmidt AM, Creager MA. Advanced glycation end products: Sparking the development of diabetic vascular injury. Circulation. 2006; 114(6): 597-605. doi: 10.1161/CIRCULATIONAHA.106.621854
7. The American Diabetes Association Releases the Standards of Care in Diabetes-2024. Accessed May 29, 2025. https://diabetes.org/newsroom/press-releases/american-diabetes-association-releases-standards-care-diabetes-2024
8. Pandey KB, Rizvi SI. Plant polyphenols as dietary antioxidants in human health and disease. Oxidative Medicine and Cellular Longevity. 2009; 2(5): 270-278. doi: 10.4161/oxim.2.5.9498
9. Nizamuddin SFS. Polyphenol-rich black chokeberry (*Aronia melanocarpa*) and its therapeutic potential in type 2 diabetes mellitus: A comprehensive review. Mediterranean Journal of Medicine and Medical Sciences. 2025; 1(3): 31-42. doi: 10.5281/zenodo.17619107
10. Scalbert A, Manach C, Morand C, Rémésy C, Jiménez L. Dietary polyphenols and the prevention of diseases. Critical Reviews in Food Science and Nutrition. 2005; 45(4): 287-306. doi: 10.1080/1040869059096
11. Manach C, Scalbert A, Morand C, Rémésy C, Jiménez L. Polyphenols: Food sources and bioavailability. The American Journal of Clinical Nutrition. 2004; 79(5): 727-747. doi: 10.1093/ajcn/79.5.727
12. Rashedinia M, Rasti Arbabi Z, Sabet R, Emami L, Poustforoosh A, Sabahi Z. Comparison of protective effects of phenolic acids on protein glycation of BSA supported by in vitro and docking studies. Biochemistry Research International. 2023; 2023: 9984618. doi: 10.1155/2023/9984618
13. Sompong W, Cheng H, Adisakwattana S. Ferulic acid prevents methylglyoxal-induced protein glycation, DNA damage, and apoptosis in pancreatic β-cells. Journal of Physiology and Biochemistry. 2017; 73(1): 121-131. doi: 10.1007/s13105-016-0531-3.
14. Oluwamodupe C, Adelabu MM, Balogun CO. Molecular docking of medicinal plants: Towards metabolic disease management. Mediterranean Journal of Medical Research. 2026; 3(3): 238-244. doi: 10.5281/zenodo.22034979
15. Jiang R, Lv Y, Chen B, Wu X, Zou Y, Liang L. Antioxidant effect of gallic acid on retinal ganglion cells in glaucoma model. Scientific Reports. 2024; 14(1): 14907. doi: 10.1038/s41598-024-65965-7
16. Maisto M, Tenore GC. Polyphenols as a useful tool to ameliorate advanced glycation end-product formation: A focus on molecular mechanisms of action. Frontiers in Bioscience (Landmark Edition). 2024; 29(12): 424. doi: 10.31083/j.fbl2912424
17. Baynes JW, Thorpe SR. Role of oxidative stress in diabetic complications: A new perspective on an old paradigm. Diabetes. 1999; 48(1): 1-9. doi: 10.2337/diabetes.48.1.1
18. Sompong W, Meeprom A, Cheng H, Adisakwattana S. A comparative study of ferulic acid on different monosaccharide-mediated protein glycation and oxidative damage in bovine serum albumin. Molecules. 2013; 18(11): 13886-13903. doi: 10.3390/molecules181113886
19. Liu JL, He YL, Wang S, He Y, Wang WY, Li QJ, et al. Ferulic acid inhibits advanced glycation end products (AGEs) formation and mitigates the AGEs-induced inflammatory response in HUVEC cells. Journal of Functional Foods. 2018; 48: 19-26. doi: 10.1016/j.jff.2018.06.024
20. Uceda AB, Mariño L, Casasnovas R, Adrover M. An overview on glycation: Molecular mechanisms, impact on proteins, pathogenesis, and inhibition. Biophysical Reviews. 2024; 16(2): 189-218. doi: 10.1007/s12551-024-01188-4
21. Vlassara H, Uribarri J. Glycoxidation and diabetic complications: Modern lessons and a warning? Reviews in Endocrine and Metabolic Disorders. 2004; 5(3): 181-188. doi: 10.1023/B:REMD.0000032406.84813.f6
22. Gkogkolou P, Böhm M. Advanced glycation end products: Key players in skin aging? Dermato-Endocrinology. 2012; 4(3): 259-270. doi: 10.4161/derm.22028
23. Twarda-Clapa A, Olczak A, Białkowska AM, Koziołkiewicz M. Advanced glycation end-products (AGEs): formation, chemistry, classification, receptors, and diseases related to AGEs. Cells. 2022; 11(8): 1312. doi: 10.3390/cells11081312
24. Umadevi S, Gopi V, Vellaichamy E. Inhibitory effect of gallic acid on advanced glycation end products induced up-regulation of inflammatory cytokines and matrix proteins in H9C2 (2-1) cells. Cardiovascular Toxicology. 2013; 13(4): 396-405. doi: 10.1007/s12012-013-9222-2
25. Yeh WJ, Hsia SM, Lee WH, Wu CH. Polyphenols with antiglycation activity and mechanisms of action: A review of recent findings. Journal of Food and Drug Analysis. 2017; 25(1): 84-92. doi: 10.1016/j.jfda.2016.10.017

26. Sompong W, Cheng H, Adisakwattana S. Protective effects of ferulic acid on high glucose-induced protein glycation, lipid peroxidation, and membrane ion pump activity in human erythrocytes. PLoS ONE. 2015; 10(6): e0129495. doi: 10.1371/journal.pone.0129495
27. Yamagishi S-I, Nakamura K, Imaizumi T. Advanced glycation end products (AGEs) and diabetic vascular complications. Current Diabetes Reviews. 2005; 1(1): 93-106. doi: 10.2174/1573399052952631
28. Rojas A, Morales MA. Advanced glycation and endothelial functions: A link towards vascular complications in diabetes. Life Sciences. 2004; 76(7): 715-730. doi: 10.1016/j.lfs.2004.09.011

Author's contribution: HSA conceived and designed the study. EAE collected data. AOJ & EAE performed data analysis and drafted the manuscript. All authors approved the final version of the manuscript and agreed to be accountable for its contents.
Conflict of interest: The authors declare the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Ethical issues: The authors completely observed ethical issues, including plagiarism, informed consent, data fabrication or falsification, and double publication or submission.
Data availability: Raw search records and data extraction forms are available upon reasonable request to the corresponding author.
Generative AI disclosure: No Generative AI was used in the preparation of this manuscript.